Clinical Medicine

Apnea of Infancy—A Clinical Problem

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Of 569 infants referred to the Children's Orthopedic Hospital and Medical Center Apnea Program (Seattle) for evaluation between 1978 and 1983, a total of 232 were discharged with cardiopulmonary monitors. Of these, 164 (71%) were at 38 weeks' gestation or more (term). In all, 203 (88%) presented with an episode in which vigorous stimulation or resuscitation was used to terminate the event. The mean age of the infants at first episode was 43 days. In 226 (97%) of the infants there was resolution of apnea symptoms by 1 year of age. During this interval, five infants died. Those infants who presented with severe episodes continued to have severe episodes at home and had a longer mean duration of monitoring than those presenting with milder symptoms.

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Presentation of an infant with a "life-threatening apneic event" continues to pose a therapeutic dilemma to the medical community. Anxious parents have found their sleeping infant cyanotic, limp and in need of vigorous stimulation or resuscitation to be revived. Although some infant apnea has a treatable cause, safety and management of those whose apnea persists remain controversial at best. Moreover, the cause remains elusive and the possible relationship to the sudden infant death syndrome ambiguous. Given the ill-defined nature of apnea, we sought to investigate the characteristics of the population referred to Children's Orthopedic Hospital and Medical Center, Seattle.

Children's Orthopedic Hospital and Medical Center is a 200-bed tertiary pediatric medical center that services Washington, Alaska, Montana and Idaho. Most of the referrals to our program, however, arise from the greater Seattle and Puget Sound basin. During the years 1978 to 1983, our program evaluated 569 infants with symptomatic apnea, siblings of victims of the sudden infant death syndrome or siblings of children with apnea. After admission to the facility, a complete history, physical and neurodevelopmental examination was completed. Laboratory investigations included chest x-ray film, electrolytes, blood gases, serum calcium and glucose levels, spinal tap, blood cultures and viral cultures when appropriate. Other specialized studies included a three-channel sleep recording and often a multichannel polysomnogram (electroencephalogram, electromyogram, electrooculogram, electrocardiogram, esophageal manometry respiratory channels, oximetry and capnography).

Following testing, those children whose apnea resolved with treatment of their underlying cause, such as sepsis, were excluded from the study. Infants with bronchopulmonary dysplasia, tracheostomies, central nervous system anomalies and maxillofacial defects were also excluded from this data base.

The remaining 232 infants (40%) were monitored. Infants included in the monitored group were those who had at least one episode of cyanosis, limpness and apnea requiring vigorous stimulation or resuscitation to restore normal breathing and in whom no treatable cause could be found. Also included in the monitored population were infants who had clinically less severe apneic episodes but whose studies showed apnea with associated bradycardia, oxygen desaturation or both.

Infants who had a sibling or first cousin with apnea and who were asymptomatic at the time of referral were monitored only if their polysomnograms showed prolonged apnea (20 seconds), bradycardia or oxygen desaturation. Only one infant, having no evidence of apnea, was monitored because of parental anxiety. She was a twin of an infant with sudden infant death syndrome.

These criteria for monitoring were not changed during the study period and, with the one exception noted above, were uniformly applied.

Results

The chronological age at presentation is presented in Figure 1, with the mean age 43 days and median age 20 days. The degree of severity of the presenting episode was also recorded. Of 232 infants, 203 (88%) infants' first episodes required vigorous stimulation or cardiopulmonary resuscitation, 8 (3.4%) required little or no intervention and 21 (9%) had no first episodes.

Within the total population mentioned, 164 (71%) were at 38 weeks' gestation or more. Premature infants made up 29% of our population. Figure 2 shows the distribution of birth

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weight among these infants. Half were between 3,001 and 4,000 grams, while 9% weighed 1,500 grams or less. Of the infants, 56% were male, 44% female and 91% were white, which is consistent with the ethnic distribution of the region. The socioeconomic status was determined by the parents' medical coverage. In all, 139 (60%) had private insurance, 65 (28%) were on medicaid and another 16 (7.5%) had Crippled Children's funding, leaving only 12 (5%) with no form of assistance. This distribution is representative of the patient population at Children's Orthopedic Hospital. Figure 3 demonstrates the range of maternal age for 214 of the infants. Most of our mothers were between 20 and 29 years of age, with a mean of 25.3 years.

TABLE 1.—*Onset Severity Versus Degree of Worst Subsequent Episode in 232 Infants With Apnea*

	Worst Subsequent Episode				
*Onset Severity**	*0*	*1*	*2*	*3*	*Died*
0, N = 21†	12	3	4	2	1
1, N = 8	2	2	4	0	0
2, N = 98	22	36	30	10	0
3, N = 105†	23	28	24	30	4

*0 = no episode, 1 = no intervention or mild stimulation, 2 = vigorous stimulation, 3 = cardiopulmonary resuscitation required.
†Including the infants who died.

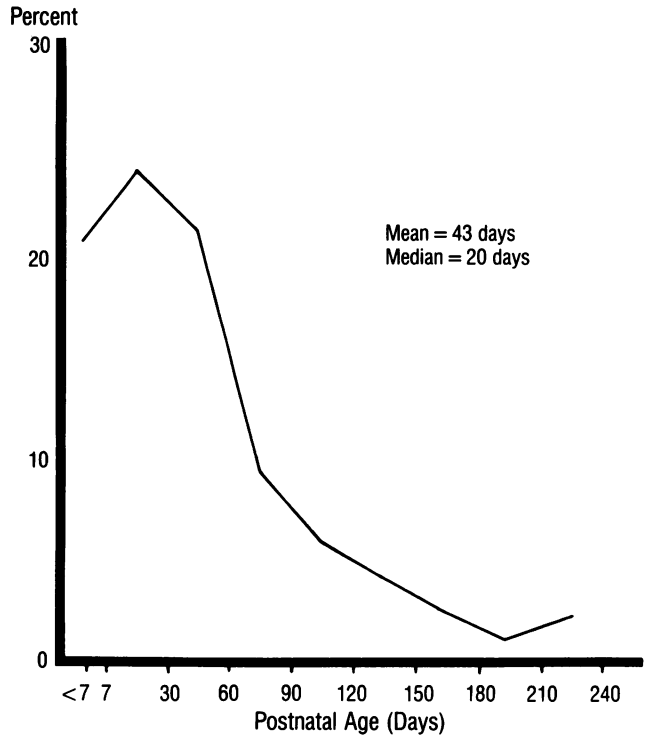

Figure 1.—Age at first observed apneic episode in postnatal days.

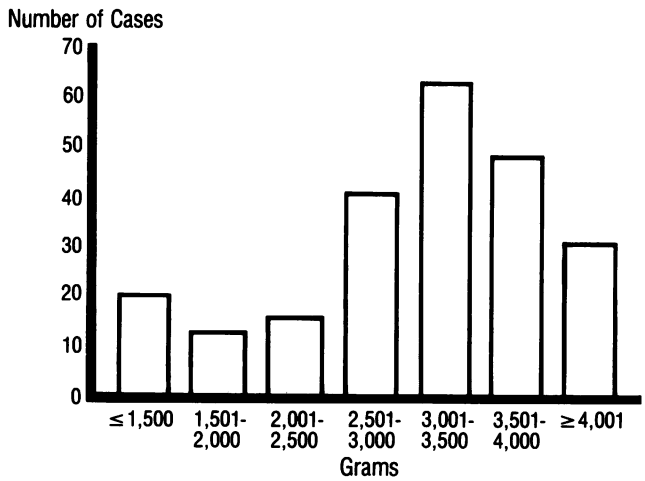

Figure 2.—Birth weight (in grams) of monitored infants (N = 227).

Follow-up

Severity of Episodes

As Table 1 shows, 65% of the infants who presented with a zero-degree or first-degree episode at onset continued to have only mild episodes. Of the 203 infants who presented with a severe episode (second and third degrees), 46% had subsequent severe episodes.

There were five deaths during the study period. Three of the infants were on their monitors at the time of death and all three monitors were functioning properly. The remaining two infants were not on their monitors the night they died. Four of the five deaths that occurred during this time were also in the most severe category (third degree) at onset. The fifth infant was a 34-week gestation baby who had no clinical episodes before being transferred to our care at 8 days of age. All of the infants who died had obstructive apneic episodes documented during polysomnograms. Factors different from the population bases in these five infants who died included a male-female predominance (4:1), family income (four out of five on medicaid), ethnic background (two minority, three white) and severity of episodes at home (one or more successful resuscitations before death). Of the three infants who had special neuropathological studies completed, all had brainstem, mid-brain or cranial nerve nuclear gliosis. Three fami-

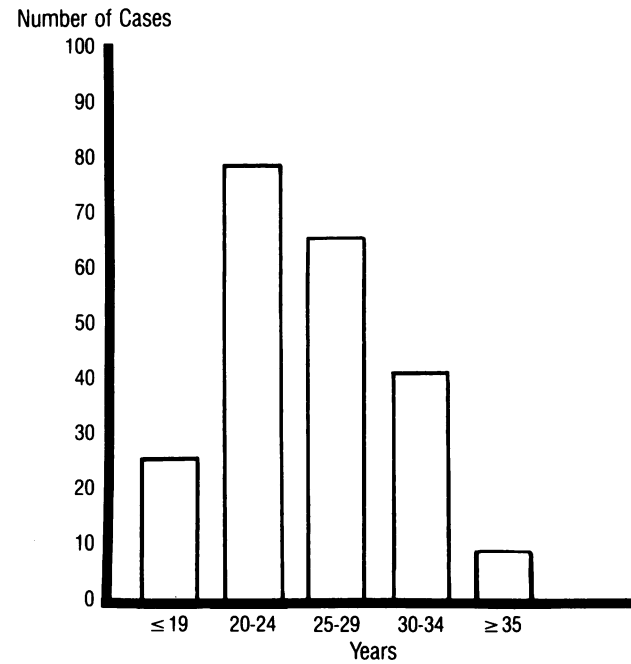

Figure 3.—Maternal age distribution of those infants monitored (N = 214).

lies also had a positive history of the sudden infant death syndrome in first-degree relatives.

Duration of Episodes

The median age of the last episode in the total population studied as reported by the parents was 90 days (see Figure 4). This included mild episodes as well as more severe episodes. Infants with parental-reported episodes beyond 1 year of age are represented by the broken line. Those infants whose presenting episode was mild (first degree) had a mean duration of episodes of 29 days, those with second degree, 78.45 days, and those with third degree had episodes lasting an average of 118 days.

Discussion

It has been difficult for clinicians, when presented with an infant with idiopathic apnea, to predict the prognosis for recurrent apneic events or, indeed, for survival. Thus, it has been necessary to make this prediction based on outcomes reported from other investigators. In a study reported by Ariagno and co-workers,[1] in 51% of infants referred to Stanford for a clinical apnea "event," no explanation for their episodes could be found. They were considered to be "at risk" for further episodes and possibly at greater risk for dying than normal infants.

For our population of referred infants, in 41% either no explanation for their episodes was found or they had persistent apneic episodes despite treatment of other problems such as gastroesophageal reflux, infections or seizures. These infants were subsequently monitored and followed.

In our population of infants followed on monitors, 71% were full term (38 weeks or more). These figures are compatible with the Stanford study.[1] The mean age at presentation was 43 days in our patients. This compares with a mean of 8.3 weeks reported by Kelly and associates,[2] 7.7 weeks reported by Ariagno and colleagues[1] and varies from a mean of 2.9 months reported by Kraus and co-workers.[3]

Our observation of the number of infants having recurrent episodes confirms earlier reports,[1,2,4] in that 88% of our infants had one or more apneic events reported after the initial evaluation. Others have reported recurrence rates as low as 43%[4] and as high as 83%.[1]

All scoring of recurrent episodes was based primarily on a parent or caretaker reporting. Parents were instructed to observe color and respirations before intervening. If mothers observed no color change, they were instructed to wait up to ten seconds before stimulating the infant. All parents were instructed to use mild to vigorous stimulation before attempting resuscitation in the presence of color change.

Of the infants receiving resuscitation, many of these episodes were corroborated by medical personnel in the hospital or by the emergency response team (Medic One). "Need for resuscitation" in many instances was suggested by the presence of hypoxia, hypercarbia or metabolic acidosis after the episode(s). If only "one or two breaths" were given to the infant and vigorous stimulation had not been given first, these cases were scored as vigorous stimulation. By this method we attempted to score resuscitations as accurately as possible. In a similar manner, we attempted to separate false alarms from episodes requiring little or no intervention. If parents reported alarms lasting four or five seconds and the infant was observed to be breathing and of normal color when parents arrived, then these events were discounted as probable false alarms. Despite this method of trying to assess the episodes and the need for intervention as accurately as possible, there are no doubt some cases where overreporting of severity or number of episodes occurred.

In all, 45% of our monitored infants had subsequent episodes requiring vigorous stimulation or resuscitation, and 12% of the infants had no reported episodes after their initial evaluation.

Of our infants, the median age at the last episode reported was 90 days. We were unable to calculate the mean age because six children (2.6%) had persistent apnea after 12

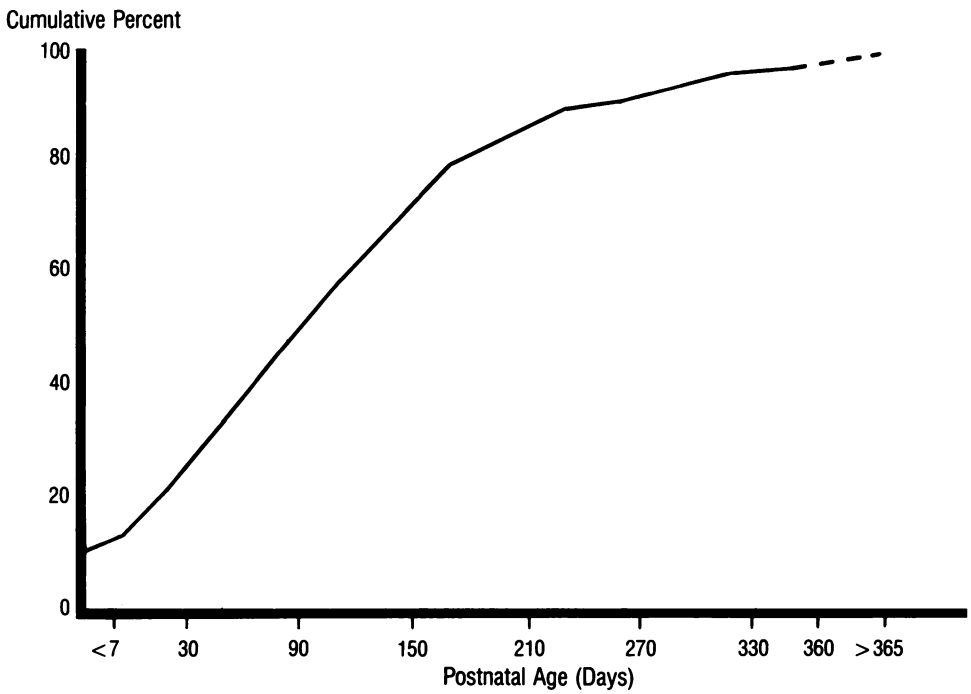

Figure 4.—Postnatal age distribution of monitored infants at last episode.

months of age and were still having episodes at the completion of the reporting year. A total of 206 (89%) infants had completed monitoring by eight months of age.

The duration from the first to the last episode was shortest for those infants presenting with mild episodes, longest for those having had one or more resuscitations and intermediate for those in between. To our knowledge, this pattern has not been reported previously and warrants further investigation.

Because there was a variable amount of time between the date of the last episode and discontinuing of monitor use, we used age at last recorded episode to more accurately describe the period of risk. All infants were monitored for at least two months after their last episode.

Subsequent deaths of a few infants with idiopathic apnea have been reported in both monitored[2] and unmonitored populations.[3,4-7]

In the absence of a controlled study, both the true magnitude of risk and the possible influence of monitoring on this risk is unknown. During the period of this study, five infants died. Maternal age, birth weight and gestational ages of the infants who died did not differ from the population as a whole. Male sex, lower socioeconomic class and ethnicity were different from the total population of infants monitored. Three infants who died were symptomatic siblings of families who had previously lost an infant to the sudden infant death syndrome. The reported mortality of such siblings who are symptomatic can be as high as 10% (D. H. Kelly, MD, oral communication, January 1985). Reported mortality rates for monitored infants varies from 0.8%[1] to 6.6%.[2] Our mortality rate of 2.1% lies between these extremes.

Summary

From our experience, we conclude that infants referred for apparently life-threatening episodes of apnea are at significant risk of further episodes and perhaps even sudden death. We recommend admission to hospital for an objective evaluation with monitoring and careful clinical follow-up for those infants in whom medical treatment fails to terminate episodes. Further follow-up studies are necessary to evaluate the possibility of long-term morbidity in those infants who have had recurrent apneic episodes.

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